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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/161,680	09/28/1998	UWE BORNSCHEUER	48429	7944

7590 01/04/2002
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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

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DATE MAILED: 01/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/161,680

Applicant(s)

BORNSCHEUER ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 02 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-7 and 11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-7 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Application Status

1. In response to the first Office action on the merits (Paper No. 17), an amendment was filed on October 2, 2001. Said action rejected all claims, Claims 1, 2, 4-7, 10, and 11.

Applicants' newly filed amendment canceled Claim 10 and amended Claims 1, 4, and 11.

Claims 1, 2, 4-7, and 11 are pending in the instant application and will be examined herein.

Priority

2. The instant application is granted the benefit of priority for the foreign application 19743683.8 filed in Germany on October 2, 1997 as requested in the declaration.

Information Disclosure Statement

3. The information disclosure statement filed on November 6, 2001 (Paper No. 19) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Drawings

4. As previously noted, the drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

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Withdrawn - Claim Objections

5. Previous objection to Claim 4 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' amendment to Claim 4.

6. Previous objection to Claim 10 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' cancellation of said claim.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

7. Previous rejection of Claims 1-2, 4-7, and 10-11 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicants' amendments.

8. Previous rejection of Claims 10-11 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicants' amendments.

Maintained - Claim Rejections - 35 U.S.C. § 102

9. Previous rejection of Claims 1-2 and 4-7 under 35 U.S.C. § 102(b) as being anticipated by Greener *et al.* is maintained. Applicants' arguments have been fully considered but are not deemed persuasive.

Applicants argue that because Greener *et al.* teach increasing an already detectable enzyme activity, this reference does not anticipate the claims as amended. The Examiner disagrees. Due to the confusing language in Claims 1, 2, and 4-7 concerning the terms activity,

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substrate specificity, and specificity, as noted in the 35 U.S.C. § 112, second paragraph rejection above, the Examiner cannot discern a difference between the art and the instant claims.

Maintained - Claim Rejections - 35 U.S.C. § 103

10. Previous rejection of Claims 1-2, 4-7, and 11 under 35 U.S.C. § 103(a) as being unpatentable over Greener *et al.* in view of Wilks *et al.* is maintained. Applicants' arguments have been fully considered but are not deemed persuasive.

Applicants argue that, contrary to the Examiner's assertion, Greener *et al.* do not teach the generation of new enzyme specificities. Applicants argue that the NADH-to-NADPH specificity switch cannot be considered a new substrate specificity because some level of NADPH specificity must have already existed in the enzyme. The Examiner notes that this is a function of enzymology in general – that all enzymes have some affinity/specificity/activity toward using a variety of substrates. The alteration of enzyme activity sites merely enhances the enzyme's potential toward particular substrates. Moreover, enzymes enhance the speed of reactions that, without enzymes, would happen anyway, albeit typically on a time scale too slow to be biologically significant. Thus, the Examiner maintains that a change in the enzyme taught by Greener *et al.* from NADH-to-NADPH, or vice versa, is just as exemplary of "new" activity as Applicants' single example in the specification.

Applicants also argue that the Examiner has misinterpreted the ADH/octanol example. The Examiner disagrees. The Examiner specifically enclosed the Abstract of Creaser *et al.* which removes all doubt of what might be a poorly written paragraph in Wilks *et al.* Creaser *et al.* state that "The enzymes with changes at two positions would metabolize both

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stereoisomerisms of 2-octanol whereas the parent ADH would attack only one of them". Thus, the unmutated ADH uses either R OR S octanol while the mutated ADH uses BOTH R AND S octanol. Additionally, R-octanol and S-octanol are NOT the same substrate as indicated by Applicants.

Applicants also argue that the example in Wilks *et al.* is for making non-chiral enzymes while the motivation is for chiral compound synthesis. The Examiner maintains this motivation since the difference is one of semantics considering the random mutagenesis methods utilized.

Applicants argue, on page 8 of their remarks, that "creating an enzyme having a 'new' substrate specificity, specifically given the generally more complex changes potentially involved, depends mainly on the degree to which the framework of the enzyme has been studied and understood." This statement is in contradiction to original arguments presented by Applicants in response to enablement rejections set forth previously in prosecution. The Examiner suggests perhaps limiting the claim language to more simple enzymes since clearly Applicants are concerned about the effectiveness of their random methods where complex enzymes are used.

Applicants argue that Greener *et al.* and Wilks *et al.* would lead the skilled artisan away from the random techniques claimed. While this may be true of more efficient and more productive "new" enzyme production, random methods are typically embraced by skilled artisans for their ease and likelihood of more interesting results.

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NEW REJECTIONS

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 2, 4-7, and 11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification loosely defined "substrate specificity" in the following sentence from page 4, lines 1-3: "The alteration in the substrate specificity reduces the K_m or increases the k_{cat} , or both, i.e. the ratio k_{cat}/K_m becomes greater than zero." As the Examiner has previously noted, the art defines substrate specificity by k_{cat}/K_m ; the "greater than zero" phrase in the specification is unclear. In Claim 1, the first 4 lines describing the method are unclear in view of this definition. Firstly, the terms "substrate specificity" and "specificity" seem to be used interchangeably in Claim 1; however, in the art, the term "specificity" has a much broader definition. The correct definition for the claims is unclear. Secondly, the phrases "on which" and "on that" in lines 2 and 3, respectively, are wholly unclear as to the intent of the prepositional phrases. Particularly, these phrases confuse the definition of specificity more since they indicate, to the best of the Examiner's ability to interpret the claims, enzyme activity, not specificity. Lastly, the idea of detection is not clear as to its metes and bounds, particularly because some methods of detection are more sensitive than others and because new methods of detection are constantly being developed.

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Conclusion

12. Claims 1, 2, 4-7, and 11 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


PONNATHAPACHUD MURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1800

KMK
January 2, 2002